

ETA-N patients were excluded from the analysis owing to an insufficient number of data points. mHAQ, pain scores, and morning stiffness improved significantly in ETA-N patients, whereas no improvement was noted among the group of ETA-F patients, in the first year after they were receiving IFX. Six ETA-F and seven ETA-N patients discontinued treatment after 4 and 5.7 months, respectively. No significant difference in the number of adverse events was found between ETA-F and ETA-N patients.

We also analysed the functional change and rate of adverse events among patients with RA treated with IFX for those receiving concomitant methotrexate (MTX-R) and those not (MTX-NR). Baseline age and disease duration of MTX-R and MTX-NR patients were similar. IFX treatment was discontinued in 15/42 (36%) MTX-R subjects and 12/46 (26%) MTX-NR subjects. After an average of 6.7 months' follow up 40/61 subjects experienced 96 adverse events (AEs) over a total of 648 infusions; 16/27 (59%) MTX-NR subjects had 46 AEs, compared with 24/34 (71%) MTX-R subjects who had 50 AEs ($p=0.51$). Most of these AEs were minor and none resulted in IFX discontinuation. There was no difference in mHAQ, pain score, swollen and tender joint counts between the MTX-R and MTX-NR groups after 6 months of treatment.

Our clinical experience demonstrates a better clinical response to IFX among ETA-naïve patients. Based on our data, we would suggest that if ETA fails there might not be a substantial benefit in trying IFX later on. Also, we did not note any difference in the rates of discontinuation or AEs, or response to treatment between MTX-R and MTX-NR patients beyond 6 months of IFX treatment.

We are limited by the number of our patients, just as van Vollenhoven *et al* were. We also do not have data for patients who switched from IFX to ETA because of the shortage of ETA at the time of our study. These results may reflect a population of refractory patients with RA who have more severe disease (patients for whom multiple DMARDs had failed) and are generally difficult to manage, or who are non-anti-TNF responders. Analysis of ETA-F patients who respond to IFX may show a subgroup who will benefit from different anti-TNF formulations. Given the cost of anti-TNF drugs, larger groups should be studied to determine the characteristics of patients who might benefit from a trial of another anti-TNF agent when one has already failed.

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Author's reply

We genuinely appreciate Drs Yazici and Erkan's interest in our paper.¹ The observa-

tions they report based on their own infliximab registry are very interesting indeed. In that registry, patients for whom etanercept treatment had previously failed responded less well to treatment with infliximab than etanercept-naïve patients. This is not, in itself, a contradiction to our published report, the gist of which was that patients can have meaningful and significant responses to infliximab even if they failed to respond to etanercept—without making a direct comparison with the results seen in etanercept-naïve patients. However, it would be of interest to know more details about Drs Yazici and Erkan's patient group.

For instance, the fact that 15 of 21 patients who were said to be "non-responders" continued treatment with infliximab suggests that some measure of improvement was none the less achieved. We have previously published data showing that a sharp distinction between "responders" and "non-responders" is an artefact and that responses in fact are normally distributed.²

Yazici and Erkan also suggest that infliximab with or without concomitant methotrexate provides similar clinical results. In our own database only a few patients received infliximab without concomitant methotrexate so we cannot provide any data bearing directly on this issue. We do note, however, that the important radiological benefits of treatment with infliximab have only been documented in patients receiving background methotrexate.³ Thus, we continue to favour this combination when possible.

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Seronegative antiphospholipid syndrome

I agree with Hughes and Khamashta that the use of the term "seronegative antiphospholipid syndrome (APS)" is useful in clinical practice.¹ However, the analogy with seronegative rheumatoid arthritis and antinuclear antibody (ANA) negative lupus is not correct. The current criteria for the classification of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) allow the diagnosis of RA or SLE to be made even if the rheumatoid factor or the ANA is negative, and therefore, seronegative RA and ANA negative SLE are embraced within the classification criteria and as such are not separate entities.^{2–4}

In the case of APS (Hughes' syndrome), the current preliminary classification criteria do not allow a diagnosis of APS to be made in the absence of at least two positive tests for either anticardiolipin antibodies or lupus anticoagulant at least 6 weeks apart.⁵ A revised international consensus statement on classification criteria for APS (Hughes' syndrome) is required to accommodate the seronegative clinical entity.

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Authors' reply

We take Dr Jawad's points and agree fully. We also believe that classification criteria are too often wrongly used in diagnosis. Our aim in writing the leader¹ was to highlight what we believe to be a not uncommon diagnostic situation—the patient with many of the features of the syndrome in whom tests remain stubbornly negative.

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Ibandronate and prevention of postmenopausal osteoporosis

Stakkestad *et al* reported a clinical trial where intravenous (IV) ibandronate injections, given every 3 months during 1 year, produced a dose dependent gain in mean (SD) lumbar spine bone mineral density (BMD) compared with placebo in prevention of bone loss in postmenopausal women.¹ The treatment was then proposed as an alternative to oral bisphosphonates and hormonal therapy in preventing postmenopausal osteoporosis.

The primary outcome was the relative change from baseline in lumbar BMD after 2 years of treatment tested by analysis of